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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,960	05/09/2005	Bill Clark	PN0222	7113

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GE HEALTHCARE, INC.
IP DEPARTMENT 101 CARNEGIE CENTER
PRINCETON, NJ 08540-6231

EXAMINER	
KILPATRICK, BRYAN T	

ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
05/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,960	CLARK ET AL.	
	Examiner	Art Unit	
	BRYAN T. KILPATRICK	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *2-5,9-24 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-8,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The arguments/remarks filed on 15 February 2010 have been entered and fully considered.

2. Instant claims 2-5, 9-24, and 26 have been withdrawn from further consideration, and instant claims 1, 6-8, 25, and 27 are pending currently.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed **terminal disclaimer** in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6-8, 25, and 27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-16 of copending Application No. 10/311,108 in view of W. O. 01/96895 (COOK et al.).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and claims 13-16 of copending Application No. 10/311,108 recites a method of analysis for a biological system containing at least one NMR active nuclei that a.) hyperpolarizes the NMR active nuclei, b.) generates a pattern for the system or samples extracted from the system using NMR analysis, c.) subjects the system to a change by introducing a drug, d.) further hyperpolarizes the NMR active nuclei, e.) generates a pattern for the system or samples extracted after introducing the drug, and f.) compares the NMR patterns for systems to identify any changes in NMR patterns. It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the method of copending Application No. 10/311,108 for the purpose of observing protein activity after the introduction of a drug into a biological system since there is evidence that protein activity in biological systems can be observed. COOK et al. discloses “evaluating drug efficacy and safety currently include measurements of responses of living systems to drug candidates either at the genetic level or at the level of expression of cellular proteins, using so-called genomic and proteomic methods respectively” on p. 4, lines 1-5.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6-8, 25, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over W. O. 01/96895 (COOK et al.), and further in view of W. O. 00/40988 (ARDENKJAER-LARSEN et al.).

In regards to instant claim 1, COOK et al. recites a method of analysis for a biological system containing at least one NMR active nuclei that a.) hyperpolarizes the NMR active nuclei, b.) generates a pattern for the system or samples extracted from the system using NMR analysis, c.) subjects the system to a change by introducing a drug, d.) further hyperpolarizes the NMR active nuclei, e.) generates a pattern for the system or samples extracted after introducing the drug, and f.) compares the NMR patterns for systems to identify any changes in NMR patterns (claims 13-16). COOK et al. further discloses in paragraphs [0013]-[0014] that the method employs DNP as a method of polarizing NMR active nuclei, as well as the use of the same NMR nuclei in claim 4. Furthermore, regarding protein activity in biological systems, COOK et al. discloses "evaluating drug efficacy and safety currently include measurements of responses of living systems to drug candidates either at the genetic level or at the level of expression of cellular proteins, using so-called genomic and proteomic methods respectively" on p. 4, lines 1-5.

COOK et al. does not expressly disclose the use of with at least two probe compounds containing at least one of C^{13} and N^{15} NMR active nuclei and acting as substrates, inducers, or inhibitors of a protein. However, ARDENKJAER-LARSEN et al. discloses the use of oligonucleotide or polynucleotide probes enriched with

hyperpolarized nuclei to target specific areas of biological samples for acquiring specific information (page 15, lines 21-30). ARDENKJAER-LARSEN et al. further discloses assays encompassing methods such as competition and binding assays that employs enzyme-substrate inhibitors or reactions, nuclease assays, etc. (page 7, lines 13-19). Since both COOK et al. and ARDENKJAER-LARSEN et al. recite methods of observing biological systems, it would have been obvious to one of ordinary skill in the art to modify the method of COOK et al. to employ the probes of ARDENKJAER-LARSEN et al. for the purpose of observing whether or not probes have bound to a biological sample (page 15, lines 21-30 of ARDENKJAER-LARSEN et al.) after the introduction of a drug (claims 13-16 of COOK et al.).

In regards to instant claim 6, COOK et al. recites a method of analysis for urine sample in claim 12.

In regards to instant claims 7-8, 25, and 27; ARDENKJAER-LARSEN et al. teaches that “biological species” is one that is present in living systems, or that is introduced into and is reactive with such systems in lines 8-9 of page 4. The prior art also teaches an assay method for analyzing biological macromolecules such as proteins, e.g., enzymes, receptors, DNA, RNA binding proteins, and carrier proteins (similar to cytochrome); olignucleotides such as DNA and RNA probes; macrocyclic molecules such as cyclodextrin; carbohydrate macromolecules; and lipids (page 4, lines 10-13). The prior art further teaches assays encompassed by the disclosed method such as enzyme-substrate inhibitors, nuclease assays, etc. (page 7, lines 13-19).

Even though ARDENKJAER-LARSEN et al. does not explicitly disclose the compounds recited in instant claims 7-8, 25, and 27, the description of "biological species" taught by the prior art describes the compounds recited by the instant claims. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use compounds as biological species for the purpose of observing physical or chemical changes as disclosed in lines 6-7 of page 4.

Response to Arguments

Applicants' arguments/remarks filed 15 February 2010 have been fully considered but they are not persuasive.

In regards to Applicants' remarks regarding the nonstatutory obviousness-type double patenting rejection over claims 13-16 of copending Application No. 10/311,108, Applicants state, "There is no indication in the cited claims of a method for monitoring the effect of a putative drug on selected proteins or even family proteins…" on p. 3 of the remarks. Claims 13-16 of copending Application No. 10/311,108 recite a method of investigating a biological system that has been subjected to a change caused by the introduction of a drug; furthermore, it is well known in the art that "proteins or even family proteins" are encompassed by "biological system." Applicants state, "Furthermore, application no. 10/311,108 fails to disclose, teach, or suggest a method wherein at least two probe compounds enriched with ^{13}C or ^{15}N NMR active nuclei, is administered…" on p. 3 of the remarks. Claims 13-16 of copending Application No. 10/311,108 recite a method of investigating a biological system that has been subjected

to a change caused by the introduction of a drug; furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the biological system or samples extracted from the system containing at least one NMR active nuclei similarly as the at least two probe compounds enriched with ^{13}C or ^{15}N NMR active nuclei since both are samples containing NMR active nuclei that are analyzed to observe changes, as recited in the instant application and pending application claims.

In regards to Applicants' remarks regarding the rejection of independent instant claim 1 (and its dependent claims - 6-8, 25, and 27) under 35 U.S.C. 103(a) over the combination of COOK et al. and ARDENKJAER-LARSEN et al, Applicants state that neither COOK et al. nor ARDENKJAER-LARSEN et al. discloses, either in combination or singularly, a method of determining protein activity of a protein or family of proteins present in a biological system on p. 4-6 of the remarks. COOK et al. recites, "…investigating the state of a biological system containing at least one NMR active nuclei…" and "…analysing the system or sample extracted from the system…" in claims 13-17, and and further discloses observing activity at the cellular protein levels of living systems after introducing drug candidates (p. 4, lines 1-5).; thereforeTherefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the claimed invention of COOK et al. similarly as the invention of the instant application. ARDENKJAER-LARSEN et al. discloses the use of oligonucleotide or polynucleotide probes enriched with hyperpolarized nuclei to target specific areas of biological samples for acquiring specific information (page 15, lines 21-30).

ARDENKJAER-LARSEN et al. further discloses assays encompassing methods such as competition and binding assays that employs enzyme-substrate inhibitors or reactions, nuclease assays, etc. (p. 7, lines 13-19). Since COOK et al. discloses the use of drugs as a "test compound" that may be exogenous or endogenous to a biological system being studied (p. 1, lines 13-18 of COOK et al.), it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the enriched probes of ARDENKJAER-LARSEN et al. for the purpose of studying protein activity in biological systems.

Applicant's arguments/remarks, see p. 2-3, filed 15 February 2010, with respect to the rejection(s) of claim(s) 1, 6-8, 25 and 27 under nonstatutory obviousness-type double patenting have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of 13-16 of copending Application No. 10/311,108 in view of W. O. 01/96895 (COOK et al.) - see rejection above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRYAN T. KILPATRICK whose telephone number is (571)270-5553. The examiner can normally be reached on Monday - Friday, 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797

/B. T. K./
Examiner, Art Unit 1797